REMARKS

Reconsideration and withdrawal of the rejections of the pending claims are respectfully requested in view of the remarks herein, which place the application in condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1, 2, and 4-23 remain pending in this application.

Claim 24 has been added, support for which can be found, for example, in ¶ 0043-0050 of the application as published.

Claim 1 has been amended to include the recitation of propylene glycol, citric acid, and anhydrous citric acid, support for which can be found, for example, in ¶ 0040, 0048 of the specification of the application as published. Additional support for this recitation can be found on page 6 of the provisional application (US 60/530,939).

Claim 1 has also been amended to delete the recitation of milbemycin and to replace the recitation of the pH range with the recitation of a percentage range for the additional stabilizer, support for which is found in ¶ 0041 of the specification of the application as published. Additional support for this recitation can be found on page 9 of the provisional application (US 60/530,939).

Claim 2 has been amended to delete the recitation of milbemycin in order to conform to claim 1.

Claim 12 has been amended in order to depend on claim 1, rather than claim 11. Support for which can be found, for example, in ¶ 0037, 0041, and 0043-0050 of the specification of the application as published.

Claim 13 has been amended to include the recitation of ivermectin, propylene glycol, citric acid, and anhydrous citric acid, support for which can be found, for example, in ¶ 0040, 0048 of the specification of the application as published. Additional support for this recitation can be found on page 6 of the provisional application (US 60/530,939).

Claim 13 has also been amended to include the recitation of a percentage range for the additional stabilizer, support for which is found in ¶ 0041 of the specification of the application as published. Additional support for this recitation can be found on page 9 of the provisional application (US 60/530,939).

Claim 17 has been amended to delete the recitation of milbemycin and the pH range.

Claim 18 has been amended to delete the recitation of milbemycin.

Claim 24 has been added to recite specific embodiments of the premix, support for which is found, for example, in ¶ 0043-0050 of the specification of the application as published. Additional support for this recitation can be found on pages 9-10 of the provisional application (US 60/530,939).

It is submitted that the amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, these amendments are made simply for clarification.

The issues raised by the Examiner in the Advisory Action are addressed below in the order they appear in the prior Action.

II. PRIORITY OF THE APPLICATION

The Examiner maintains that the instant application is not entitled to the benefit of priority of the provisional application filed December 19, 2003 (60/530939, hereinafter referred to as the '939 application), asserting that it does not "provide support for the instant compositions and methods within the full scope of the present claims" of the subject application filed March 1, 2004. In particular, the pH range was cited by the Examiner as being allegedly unsupported by the provisional application.

The attention of the Examiner is drawn to the '939 application, in which the concentration ranges of avermectin (or derivative thereof), oil/surfactant, wax, antioxidant and carrier are all listed in the specification on pages 6, 9 and 10, as well as in claim 11. The recitation of the concentrations each of these components in the '939 application is consistent with those recited in the present application.

The current claims have been amended to remove the recitation of the pH range, and replace with percentage ranges of the ingredients. Support for which can be found, for example in the '939 application on pages 5-7, 9-10, claims 11-13, and claim 18.

Thus, the subject application as amended is reflective of the ranges of the ingredients recited in the provisional application, and the applicants request confirmation as to the priority date of December 19, 2003, which is the filing date of U.S. Provisional Application No. 60/530,939, the '939 application.

III. THE REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, ARE OVERCOME

Claims 1, 2 and 4-23 remain rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner contends that guidance is not provided as to other combinations wherein a milbemycin or different stabilizer is employed that would be reasonably expected to demonstrate extension of shelf life of various avermectins and milbemycins. Further, it is stated that no direction is provided to distinguish among the various stabilizers that appear to be the most critical element in extending shelf life of the product, which forces extensive testing of formulary combinations by the skilled artisan. Applicants respectfully disgree.

According to the Court of Appeals for the Federal Circuit in the case of *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988),

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. 'The key word is undue, not experimentation.' The determination of what constitutes undue experimentation in a given case requires the application of standard of reasonableness, having due regard for the nature of the invention and the state of the art. The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed ... [Citations omitted]. *Id.* at 1404.

The Examiner is respectfully reminded that considerable experimentation is permissible if said experimentation is routine or if the specification provides reasonable guidance with respect to the direction in which experimentation should proceed.

Applicants respectfully assert that the specification provides reasonable guidance regarding the direction of experimentation to one skilled in the art.

It is appreciated by one skilled in the art that ivermectin (the avermectin derivative used in Example 1) is representative of the avermectin/milbemycin structural class (the Examiner's attention is directed to US 7,001,889 and references therein). Paragraphs 0036-0039 in the instant specification outline the common structural features between the avermectins and milbemycins which are liabilities with respect to decomposition. Thus, from the information in the specification in conjunction with inherent skill in the art, it is readily apparent that the current

formulation invention is applicable to any member of the avermectin/milbemycin family of macrocyclic lactones by routine substitution of any of these family members for ivermectin in the example provided.

Applicants also respectfully disagree that no direction is provided to distinguish among the various stabilizers critical in extending shelf life. As one skilled in the art will appreciate, the stabilizers referred to in the specification (paragraphs 0038 and 0039) serve the function of stabilizing the formulation by increasing the concentration of the hydrogen ion in solution. One skilled in the art of chemical formulations has sufficient background in acid/base chemistry to realize that substitution of any pharmaceutically acceptable acid may be applied to the exemplified formulary to serve the same purpose of changing hydrogen ion concentration. This experimentation is routine, and the example in the specification provides adequate direction toward which one skilled in the art may proceed.

The current invention teaches the extension of shelf life by decreasing or preventing acid or base catalyzed decomposition of avermectin and milbemycin derivatives by controlling the amount of stabilizer in the premix formulation in an amount effective to buffer the acidity thereby minimizing decomposition. The subject application provides methods for successful stabilization and extension of shelf life of the claimed formulations by describing the formulation and providing for the addition of a stabilizer in order to prevent decomposition. Recognizing that the avermectin/milbemycin family is of the same structural class, one skilled in the art will also recognize that the example provided in the specification may be extended to incorporate any member of the avermectin/milbemycin family of macrolides. Similarly, the skilled artisan will appreciate that the stabilizer exemplified functions as an acid/base and substitution of other acids/bases will function similarly to achieve the same result. Thus, the use of the composition described provides full enablement for one skilled in the art to practice said invention.

In view of the statements above, the breadth of the claims is not unduly broad, the amount of direction provided by the instant specification is high, particularly in regard to the inclusion of the working example, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure is therefore low and, in any event, would not constitute undue experimentation.

Although applicants respectfully disagree with the Examiner, in the interest of expediting prosecution, the claims have been amended to remove the recitation of milbemycin derivatives

and specify the stabilizer as an acid. Further clarification has been provided as the amended claims recite specific ingredients, rather than referring to waxes, surfactants, antioxidants, and carrier vehicles in general. As such, the claims fully enable to skilled artisan to make and use the current invention.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, are respectfully requested.

III. THE REJECTIONS UNDER 35 U.S.C. § 103(a) ARE OVERCOME

Claims 1-23 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Beuvry et al., U.S. Patent No. 5,824,653, in view of Katoh et al., U.S. Patent No. 4,939,166, Chabala et al., U.S. Patent No. 4,199,569, Sutherland et al., U.S. Patent No. 4,910,219, Freehauf et al., U.S. Patent No. 7,001,889, and Carson et al., U.S. Patent No. 6,548,478. Applicants respectfully disagree.

Establishing a *prima facie* case of obviousness requires that the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP 2143.

The Examiner is respectfully reminded of the case law, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). As stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Office Action does not make the modification obvious unless the prior art suggests the desirability of the modification." Furthermore, the Supreme Court has recently reaffirmed the factors set out in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18: "[T]he scope and content of the prior art are determined; differences between the prior art and the claims at issue are...ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___ (2007).

According to the instant claims, none of the references cited teach, suggest, motivate or render obvious to try the presently claimed invention of increasing the amount of existing stabilizer in the premix in order to increase stability and shelf life of the feed.

Unexpected results are presented in Tables II and III of the present application, wherein the example is given of additional stabilizer being added to the Ivomec premix. A small amount (between 0.3 and 1.2%) of added stabilizer provides a significant benefit with respect to minimization of degradation and extension of shelf life relative to the original Ivomec premix. This provides a clear example of the present application addressing an unsolved problem in the context of avermectin formulations for premixes.

For the foregoing reasons, none of the references cited by the Examiner, either alone or in combination, render the pending claims *prima facie* obvious. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) are respectfully requested.

REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, an interview with the Examiner and SPE is respectfully requested, prior to issuance of any paper other than a Notice of Allowance; and, the Examiner is respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.

CONCLUSION

For the reasons stated above, Applicants respectfully request a favorable reconsideration of the application, reconsideration and withdrawal of the rejections of the pending claims, and prompt issuance of a Notice of Allowance.

Respectfully submitted,
MERIAL LTD.
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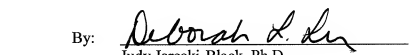
By: 

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